

2014-1545

(Serial No. 12/528,118)

BEFORE THE UNITED STATES COURT OF APPEALS

FOR THE FEDERAL CIRCUIT

IN RE CLAIRE RODRIGUEZ-LAFRASSE AND ELIE HADCHITY

Appeal from the United States Patent and Trademark Office

Patent Trial and Appeal Board

BRIEF FOR APPELLANT

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Certificate of Interest

Counsel for the Appellant, certifies the following:

1. The full name of any party or amicus represented by me is:

CLAIRE RODRIGUEZ-LAFRASSE AND ELIE HADCHITY

2. The name of the real party in interest (if the party in the caption is not the real party in interest) represented by me is:

The University of British Columbia (assignee)

OncoGenex Technologies Inc. (licensee)

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

OncoGenex Pharmaceuticals, Inc. (a public company) owns 100% of OncoGenex Technologies Inc.

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court are:

Marina T. Larson, Ryan E. Anderson, Allison Olenginski

Larson & Anderson, LLC

Table of Contents

<u>Certificate of Interest</u>	-i-
<u>Table of Authorities</u>	-iii-
<u>Statement of Related Cases</u>	-1-
<u>Appellate Jurisdiction Statement</u>	-1-
<u>Issues Presented for Review</u>	-2-
<u>Statement of the Case</u>	-3-
<u>Statement of the Facts</u>	-4-
<u>Summary of Argument</u>	-8-
<u>Argument</u>	-11-
Standard of Review.....	-11-
The Claimed Invention is Not Obvious Over the Entirety of the Record	-11-
The PTAB’s Decision to Consider Less Than the Full Record is Not Supported by Substantial Evidence	-15-
The PTAB’s Reasons for Considering Less Than the Full Record Was a New Ground of Rejection.....	-20-
Conclusion.....	-24-
Copies of Decisions of PTAB	-25-
Certificate of Service.....	

Table of Authorities

Cases Cited

<i>In re Gartside</i> , 203 F.3d 1305, 1316 (Fed.Cir.2000).....	-11-
<i>In re Lamberti</i> , 545 F.2d 747 (C.C.P.A. 1976).	-16-
<i>Custom Accessories, Inc. v. Jeffrey-Allan Indust., Inc.</i> , 807 F.2d 955 (Fed Cir. 1986).	-15-
<i>Graham v. John Deere Co. of Kan. City</i> , 383 U.S. 1 (1966).	-11-
<i>In re Biedermann</i> , 733 F.3d 329 (Fed. Cir. 2013).	-21-
<i>In re Dow Chemical</i> , 837 F.2d 469 (Fed. Cir. 1988).	-16-
<i>In re Kumar</i> , 418 F.3d 1361 (Fed. Cir. 2005).....	-21-
<i>In re Leithem</i> , 661 F.3d 1316 (Fed. Cir. 2011).....	-20-, -21-
<i>In re Oetiker</i> , 977 F. 2d 1443 (Fed Cir. 1992).	-9-
<i>In re Soni</i> , 54 F.3d 746, 750 (Fed.Cir.1995)	-15-
<i>In re Stepan Co.</i> , 660 F. 3d 1341 (Fed. Cir. 2011).....	-11-
<i>In re Sullivan</i> , 498 F. 3d 1345 (Fed. Cir. 2007).....	-15-
<i>In re Young</i> , 927 F.2d 588 (Fed Cir. 1991).....	-17-
<i>Rambus Inc. v. Rea</i> , 731 F. 3d 1248 (Fed. Cir. 2013).....	-22-
<i>Standard Oil Co. v. American Cyanamid Co.</i> , 774 F.2d 448 (Fed. Cir. 1985)	-15-

Statutes Cited

28 U.S.C. § 1295 (4)(A).....	-1-
35 U.S.C. § 103(a)..	-2-, -4-, -9-, -24-

Regulations Cited

37 CFR 41.50(b).	-2-, -11-
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Statement of Related Cases

Pursuant to the provisions of Federal Circuit Rule 47.5, Appellants are not aware of any related cases.

Appellate Jurisdiction Statement

This is an Appeal from the Decision of the United States Patent and Trademark Office, Patent Trial and Appeal Board mailed January 18, 2014, maintained in the Decision on Request for Rehearing mailed March 27, 2014. This Court has jurisdiction under 28 U.S.C. § 1295 (4)(A).

This Appeal was timely filed on May 7, 2014.

The Decision of the Patent Trial and Appeal Board dated January 18, 2014, as maintained in the Decision on Request for Rehearing mailed March 27, 2014, is a final decision.

Issues Presented for Review

Two issues are presented for review, with the second being presented in the alternative.

The first issue presented is whether the art of record provides a sufficient basis for the rejection of claims 1, 2, 6, 13 and 15 as unpatentable under 35 U.S.C § 103(a). Appellants submit that the art is not sufficient, and therefore that the rejection should be reversed.

The second issue, presented in the alternative, is whether the Decision on Appeal mailed January 18, 2014 and the Decision on Request for Rehearing mailed March 27, 2014 are improperly based on a new ground of rejection to which Appellants were not given fair opportunity to respond. If the decision that the claimed invention would have been obvious is not reversed, then Appellants request that the case be remanded to the Patent Trial and Appeal Board with instructions to designate the 35 U.S.C. § 103(a) rejection as a NEW GROUND OF REJECTION in accordance with the provisions of 37 CFR 41.50(b).

Statement of the Case

This case is an Appeal from the Decision of the Patent Trial and Appeals Board ("PTAB") dated January 18, 2014 (hereinafter "Decision").

(A1-20) In the Decision, rejections of claims 1-6 and 13-17 were reviewed and affirmed in-part and reversed in-part.

The rejections of claims 1, 3, and 17 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirements were reversed.

(A3-7)

The rejections of claims 1-6 and 13-17 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement were reversed.

(A7-12)

The rejections of claims 1, 2, 6, 13 and 15 under 35 U.S.C. § 103(a) were affirmed. (A12-20) This rejection and the affirmance thereof is the subject of this Appeal.

A Request for Reconsideration was filed on March 17, 2014 and a Decision on Request for Rehearing Decision (A21-24) (hereinafter "Rehearing Decision") was mailed on March 27, 2014.

Statement of the Facts

The claims on Appeal in this case (A26) are directed to a method for treatment of squamous cell carcinoma (SCC) using a combination of radio-therapy and a therapeutic agent that reduces the amount of hsp27 in squamous cancer cells. Independent claim 1 is representative and reads:

1. A method for treatment of squamous cell carcinoma characterized by elevated expression of hsp27 as compared to non-cancerous cells of the same type in an individual suffering from the cancer, comprising treating a patient diagnosed with a squamous cell carcinoma with a combination of radio-therapy and a therapeutic agent that reduces the amount of hsp27 in the squamous cancer cells.

Both the Examiner and the PTAB found that “the state of the art linking a reduction in the overexpression of hsp27 and treatment of squamous cell carcinoma was unpredictable.” (FF12, A9).

Claims 1, 2, 6, 13 and 17 were rejected by the Examiner under 35 U.S.C. § 103(a) as obvious over Yonekura et al. (A269-278) and Teimourian et al. (A81-85). As found by the Patent trial and Appeal Board Yonekura teaches:

(Y1)¹ “that ‘[i]nterferon- γ (IFN- γ) is considered a likely candidate for combination therapy in anticancer drug regimes.’ ([A269]), col. 2)” (FF19, A13).

(Y2) “that a ‘number of studies indicate that ... Hsp27[] inhibits the apoptotic signaling pathway... Here, we describe a novel downregulation of Hsp27 expression in response to IFN- γ treatment of oral SCC cells.’ ([A269]), col. 2)” (FF20, A14).

(Y3) “that ‘Hsp-27 overexpressing cclones displayed resistance to cisplatin-induced apoptosis (data not shown), consistent with realrier reports. Moreover, these recombinant constructs were significantly more resistant to IFN- γ -induced cell death than control cells.’ ([A272]), col. 1).” (FF21, A14).

(Y4) “that
Hsp27 in oral SCC cells plays a critical role in the negative regulation of apoptotic cell death. IFN- γ stimulates the cell death signal via its inhibitory effect of Hsp27, although not sufficiently to cause complete apoptotic cell death. In oral SCC cells, IFN- γ

¹ For convenient group reference, these findings of fact are labeled here as Y1-Y6 for those findings relating to the Yonekura reference, T1-T4 for those findings relating to the Teimourian reference and SF1-SF4 for those findings relating to Sukuki or Fortin.

downregulates protein levels of Hsp27, and therefore possibly promotes the proapoptotic state by partially activating caspase-3 ([A273], col. 2).” (FF22, A14).

(Y5) “that ‘IFN- γ -treatment augmented apoptotic cell death caused by certain inducers, including Verotoxin and cisplatin’ ([A274], col. 1).” (FF23, A14).

(Y6) “that ‘IFN- γ alone does not induce apoptosis, probably because it does not completely terminate Hsp27 expression and function. This study at the molecular level supports the potential therapeutic benefits of a treatment strategy combining IFN- γ with other anticancer drugs, such as cisplatin’ ([A276], col. 1).” (FF24, A14).

As found by the Patent Trial and Appeal Board Teimorian teaches

(T1) “that ‘Hsp27 can also inhibit apoptosis through the direct inhibition of caspase activation’ ([A81], col. 2).” (FF25, A15).

(T2) “that ‘down-regulation of Hsp27 in combination with radiation may serve as a useful approach to induce apoptosis in tumor cells which develops new methods for treatment of cancers. We examined the possible role of Hsp27 in cellular resistance to radiation and investigated an Hsp27 antisense as a possible radiation sensitizer’ ([A82], col. 1).” (FF26, A15).

(T3) “that:

Although DNA-damaging therapies such as γ -radiation have been widely used for the treatment of numerous cancers, cells increasingly become resistant to consecutive administration of radiation; therefore, studies involving strategies to overcome this resistance by increasing cellular sensitivity to radiation therapy contribute[] a critical step for better cancer treatments. In this study, we demonstrated that the decreased expression of Hsp27 in radioresistant prostate cancer cells produced a decline in the survival curve; this suggests a possible use of Hsp27 antisense as a radiosensitizer.

([(A84)], col. 1).” (FF27, A15).

(T4) “that ‘[i]t should again be emphasized that because overcoming radiation resistance is critical for better cancer treatment, inactivation of the stress-activated protein Hsp27 may be a promising approach to increased radiation sensitivity in cancer cells’ ([A84)], col. 2).” (FF28, A15).

The PTAB also found that:

(SF1) “Suzuki teaches that ‘[o]ur results, however, showed that the effect of chemotherapy was good in patients whose cancers overexpressed HSP-27’ ([A267)], col. 2).” (FF13, A9).

(SF2) “Suzuki teaches that ‘expression of HSP-27 seems to protect cells from apoptosis during inflammation, while down-regulation in dysplasia could impair the protective mechanism against mutagenesis induced by environmental factors, and so exaggerate the transformation of oral epithelial dysplasia into SCC’ [(A267)], col. 1).” (FF14, A9).

(SF3) “Suzuki teaches that the ‘apparent role of overexpression of HSP-27 has not been established, and remains controversial in oral SCC cells. The induction of expression of HSP-27 may prove useful in the treatment of carcinomas that do not express HSP-27’ ([A268]), col. 1).” (FF15, A9-10).

(SF4) “Fortin teaches that in ‘our study, there was a significant relationship between neck relapse and absence of HSP-27 overexpression. These results corroborate the fact that HSP-27 overexpression has been associated with good prognosis. Moreover, HSP-27 overexpression is not associated with radioresistance’ (A835, col. 2).” (FF16, A10).

Summary of Argument

Determinations of obviousness are properly made based on all of the evidence in the record, whether this be evidence of the knowledge of the person of ordinary skill in art, as reflected in printed publications, or evidence of properties

specific to a claimed invention. *In re Oetiker*, 977 F. 2d 1443, 1445 (Fed Cir. 1992) (“After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument.”) Claims are only properly rejected under 35 USC § 103(a) when this evidence considered as a whole would have suggested the claimed invention to a person skilled in the art and provided a reasonable basis for an expectation of success.

In the present case, the art of record provides evidence of different results for the role of hsp27 during treatment of squamous cell carcinoma with chemotherapy agents: one reference (Yonekura, A269-278) teaches that hsp27 inhibition is beneficial in treating squamous cell carcinoma, while another reference (Suzuki, A262-268) teaches that the presence of hsp27 is beneficial in treating squamous cell carcinoma. A secondary reference (Teimourian, A81-85) teaches that hsp27 inhibition is beneficial in the treatment of prostate cancer when combined with radio-therapy. Combination of this information without hindsight or bias leads to no suggestion to combine radio-therapy and hsp27 inhibition in the treatment of squamous cell carcinoma, because the role of hsp27 inhibition in squamous cell carcinoma is not predictable from this art. No prediction can be made of the nature of the result that would be obtained (i.e. beneficial or not) from

treating SCC by inhibiting hsp27 in combination with radiotherapy, and therefore there is no basis for asserting a reasonable expectation of success. *See, Sanofi-Synthelabo v. Apotex, Inc.*, 550 F. 3d 1075, 1088 (Fed. Cir. 2008) (prediction of which isomer would be more active was not possible in view of the art.)

The Examiner and the PTAB have considered only the parts of the record that support the rejection in arriving at the conclusion of obviousness that is appealed here. In the case of the Examiner, the consideration of only a part of the record was allegedly justified by a statement that “the Fortin reference was not relied upon in the 103 rejection of record,” and some statements on the deficiencies of the Fortin reference, with no mention of the Suzuki reference. (A909) The PTAB affirmed the rejection but offered different reasons for excluding some of the art from consideration. (A19-20) Appellants submit that the reasons offered by the PTAB do not justify the failure to consider the entire record, and that the Decision should therefore be reversed.

Appellants further submit that the reasons offered by the PTAB for excluding some of the record from consideration constitute a new ground of

rejection, to which Appellants were not given fair opportunity to respond. Thus, if the Decision is not reversed, Appellants submit that it should be vacated and remanded for treatment in accordance with the provisions of 37 CFR § 41.50(b).

Argument

Standard of Review

Obviousness is a question of law with several underlying factual inquiries. *Graham v. John Deere Co. of Kan. City*, 383 U.S. 1, 17-18 (1966). This Court reviews the PTAB’s determination of obviousness *de novo* and the factual findings underlying that determination for substantial evidence. *In re Gartside*, 203 F.3d 1305, 1316 (Fed.Cir.2000).

Whether the PTAB relied on a new ground for rejection is a legal question that is reviewed *de novo*. *In re Stepan Co.*, 660 F. 3d 1341, 1343 (Fed. Cir. 2011).

The Claimed Invention is Not Obvious Over the Entirety of the Record

Both the Examiner and the PTAB found that “the state of the art linking a reduction in the overexpression of hsp27 and treatment of squamous cell carcinoma was unpredictable.” (FF12, A9). The Yonekura reference presents results that tend to show that reduction in hsp27 expression is beneficial in the

treatment of SCC with chemotherapy. (Findings Y1-Y6 collectively, A13-14)

Suzuki presents results that show the exact opposite, i.e. that maintaining or increasing hsp27 expression is beneficial in treatment of SCC with chemotherapy.

(SF1-SF3, A9-10). Fortin teaches “in ‘our study, there was a significant relationship between neck relapse and absence of HSP-27 overexpression. These results corroborate the fact that HSP-27 overexpression has been associated with good prognosis.” (SF4, A10). Thus, two references of record teach that higher levels of hsp27 are beneficial, whilst one teaches that lower levels of hsp27 are desirable when treating SCC with chemotherapy.

Fortin 2001 also teaches that “Hsp27 overexpression has not been associated with radioresistance” although as previously noted by Appellants the citation in support of this statement in the Fortin paper is in error. Appellants now believe that the correct citation is to Fortin 2000, also of record. (A701-708).

The same statement is made in Teimourian with a citation to Fortin 2000. (A84).

The Teimourian reference teaches that reduction of hsp27 is beneficial to the treatment of prostate cancer with radiotherapy, and speculates about extensions of this observation. Teimourian makes no statements specific to SCC.

A finding of obviousness requires that a person skilled in the art would be be guided by the art to the claimed invention with a reasonable expectation of

success. “Success” in this case would be considered to be achieving a better therapeutic result in the treatment of SCC. No conclusion of obviousness can properly be reached from the entirety of the record, because there is no basis on which to arrive at a reasonable expectation that reducing the amount of hsp27 as required in the claimed invention will result in therapeutic benefit in the radiation treatment of SCC. Not only is the correlation between reduction of hsp27 and the effectiveness of chemotherapy in the treatment of SCC the subject of conflicting results, Teimourian states that “it has been shown that overexpression of Hsp27 is associated with thermoresistance and chemioresistance, but not with radioresistance.” (A84)

In this case, the Examiner argued in the context of the enablement rejection that

[t]he entire Suzuki reference, beginning with the title, is drawn to "Overexpression of heat shock protein 27 is associated with good prognosis in the patient with oral squamous cell carcinoma". From reading the reference, one of skill in the art would not predictably know that inhibition of hsp27 would be an effective treatment for scc given it has been shown that prognosis is better in a patient that overexpresses hsp27. Going to page 128 which was cited in the

rejection, Suzuki details the correlation between expression of hsp27 and chemotherapy. The art appears to be unpredictable regarding the expression of hsp27 and increased sensitivity to chemotherapeutic agents.

While it is true that the study reported by Suzuki et al. examined the correlation of patient response after chemotherapy, the fact that chemotherapy and radiation therapy are both used as secondary treatments in methods to increase the cells dysfunctional apoptotic signaling would lead one of skill in the art to question the predictability of the claimed method based on the prior art.

* * *

Therefore, one of ordinary skill in the art would not predictably know from the prior art that inhibition of hsp-27 in squamous cancer cells could be used as a treatment method along with radiation therapy. (A906-907). The interpretation of a reference by a person skilled in the art is not different depending on the nature of the rejection at issue, and thus the Examiner conceded the uncertainty in the art.

The PTAB's Decision to Consider Less Than the Full Record is Not Supported by Substantial Evidence

“When a patent applicant puts forth rebuttal evidence, the Board must consider that evidence.” *In re Sullivan*, 498 F. 3d 1345, 1351 (Fed. Cir. 2007), *citing, In re Soni*, 54 F.3d 746, 750 (Fed.Cir.1995) (stating that "all evidence of nonobviousness must be considered when assessing patentability."). Here, the rebuttal evidence is the teachings of other references in the record, that the Examiner and the PTAB deemed to be without significant weight in reaching the conclusion of obviousness. This conclusion leading to the exclusion or discounting of the Suzuki and Fortin references is a finding of fact that must be supported by substantial evidence. In the present case, it is not.

The person of ordinary skill in the art is “a hypothetical person who is presumed to be aware of all of the pertinent prior art.” *Custom Accessories, Inc. v. Jeffrey-Allan Indust., Inc.*, 807 F.2d 955, 962 (Fed Cir. 1986). *See also Standard Oil Co. v. American Cyanamid Co.*, 774 F.2d 448, 454 (Fed. Cir. 1985). Further, in determining whether such a [a suggestion [of the invention] can fairly be gleaned from the prior art, the full field of the invention must be considered; for the person of ordinary skill is charged with

knowledge of the entire body of technological literature, including that which might lead away from the claimed invention.

In re Dow Chemical, 837 F.2d 469, 473 (Fed. Cir. 1988).

Of course, the "entire body of technological literature" was not before the Examiner or the PTAB, but the Examiner improperly selected only some of the art of record in the case as the basis for the obviousness rejection and stated that consideration of the balance of the art of record was not required. The PTAB presented its own reasons for discounting the conflicting Suzuki and Fortin references.

When the prior art of record contains conflicting references, the [PTAB] must weigh each reference for its power to suggest solutions to an artisan of ordinary skill. When prior art contains apparently conflicting references, the Board must weigh each reference for its power to suggest solutions to an artisan of ordinary skill. The [PTAB] must consider all disclosures of the prior art, *In re Lamberti*, 545 F.2d 747, 750, 192 USPQ 278, 280 (CCPA 1976), to the extent that the references are, as here, in analogous fields of endeavor and thus would have been considered by a person of ordinary skill in the field of the invention. The [PTAB], in weighing

the suggestive power of each reference, must consider the degree to which one reference might accurately discredit another.

In re Young, 927 F.2d 588, 591 (Fed Cir. 1991).

The Examiner and PTAB justified their conclusion of obviousness by asserting facts to support the discrediting references other than Yonekura and Teimourian from consideration. The decision to consider only parts of the evidentiary record is in affect a determination of “the scope and content of the prior art” that leaves parts of the information out of the determination. This is only properly done if there is substantial evidence to justify the conclusion. In the present instance, these facts were not supported by substantial evidence and thus the finding of obviousness based on less than the complete record should be reversed.

The PTAB cites FF 26 and 28 (A15) as evidence that Teimourian “expressly suggests the combination of hsp27 down-regulation agents with radiation to increase radiation sensitivity of cancer cells.” (A18). These finding of fact, however, are a prefatory comment on the reasons for the experiments to be performed, and a concluding remark on what “**may** be a promising approach to increased radiation sensitivity in cancer cells.” Since Teimourian’s actual results relate only to prostate cancer and not SCC, and since Teimourian also states that

“it has been shown that over-expression of Hsp27 is associated with thermoreistance and chemioreistance, but not radioresistance,” (A84), this statement of what **may** occur is nothing but an invitation to experiment and not a prediction of the results to be obtained in any or all other types of cancer.

The PTAB also bases its decision on a statement that “Yonekura also expressly suggests combination therapy with hsp27 downregulating agents and other cancer treatments (FF24).” (A18). This statement is inconsistent with the actual statement in the reference, and in the finding of fact which refers not to “other cancer treatments” but to “other anticancer drugs, such as cisplatin.” Radiation is not a “drug” and there is no support for the effort to broaden the teaching of the reference to better fit the rejection.

The PTAB asserted “both Yonekura and Teimourian share an underlying mechanism in improving apoptosis by reducing HSP 27 levels, thereby suggesting the application of each therapeutic modality with agents which reduce HSP 27 levels. (FF 19-28)” (A18). Findings of Fact 19-28 do not provide evidence for a shared underlying mechanism of apoptosis. In fact, on their face the Yonekura and Teimourian references reflect different modalities of action vis á vis apoptosis. Teimourian states that Hsp27 may inhibit apoptosis by either of two separate mechanisms: by preventing translocation of a nuclear protein DAXX and its

binding with FAS and direct inhibition of caspase activation (A81-82). In contrast, Yonekura states that "IFNs either induce or enhance apoptosis because of inhibition of protein synthesis," (A269), a seemingly different mechanism from that described in Teimourian. Thus, the only commonality between Yonekura and Teimourian appears to be the fact that they both mention apoptosis. As found by the PTAB, however, Suzuki also mentions apoptosis, noting that 'expression of HSP-27 seems to protect cells from apoptosis during inflammation, while down-regulation in dysplasia could impair the protective mechanism against mutagenesis induced by environmental factors, and so exaggerate the transformation of oral epithelial dysplasia into SCC' (A267, col. 1)." FF14, A9. Thus, this rationale for considering only Yonekura and Teimourian is not supported by the evidence.

The PTAB asserted that Suzuki was ambiguous based on a statement that the “apparent role of overexpression of HSP-27 has not been established, and remains controversial in oral SCC cells.” (A19). This statement, even taken out of context, does not create ambiguity in the results that Suzuki reported. In context, the statement underscores the different results that have been reported in connection with Hsp27 expression in cancers of different types, and supports Appellants’ position that there is no reasonable basis for an expectation of success.

The PTAB also apparently considered it significant to its obviousness determination that Applicants had argued (in the context of the enablement rejection) that Suzuki says “absolutely nothing about radiotherapy,” (A19), but they do not say why this is significant. In fact, Yonekura does not say anything about radiotherapy either. Thus, this “fact” about Suzuki is not substantial evidence in support of the conclusion to exclude Suzuki from consideration.

The PTAB's Reasons for Considering Less Than the Full Record Was a New Ground of Rejection

In affirming the rejection of the claims in this application, the Board has articulated a new rationale for combining only Yonekura and Teimourian and excluding other references of record from consideration. This constitutes a new ground of rejection, and Appellants must be given an opportunity to respond if the rejection as a whole is not reversed.

The issue of whether a position advanced by the Patent Trial and Appeal Board constitutes a new ground of rejection has been considered by the Court in several recent cases. In general, the “ultimate criterion of whether a rejection is considered ‘new’ in a decision by the Board is whether applicants have had fair opportunity to react to the thrust of the rejection.” *In re Leithem*, 661 F.3d 1316,

1319 (Fed. Cir. 2011). Mere reliance on the same statutory basis and the same prior art references, alone, is insufficient to avoid making a new ground of rejection when the Board relies on new facts and rationales not previously raised to the applicant by the examiner. *Leithem* at 1319, citing *In re Kumar*, 418 F.3d 1361, 1367-68 (Fed. Cir. 2005). Comparison of the circumstances in this case with those in various cases previously considered by this Court makes it clear that a new ground of rejection was relied upon by the PTAB in this case.

In *Leithem*, a new ground of rejection was found because of a change in a characterization of a reference as disclosing fluffed pulp to a characterization that the reference disclosed pulp that could be fluffed. In *In re Biedermann*, 733 F.3d 329, 337-338 (Fed. Cir. 2013),

the examiner's reasoning in support of combining the square thread of Steinbock with the device of Cotrel was that there were a limited number of threads that could be used and that a square thread was the most efficient...The Board, on the other hand, found new facts as the basis for concluding that the combination of Cotrel and Steinbock would have been obvious: that Cotrel teaches avoiding splaying with saw-tooth threads; that saw-tooth threads are buttress threads; that

Steinbock groups together the square threads and buttress threads;
and that square threads avoid splaying.

This Court concluded that this was a new ground for rejection. Similarly, in *Rambus Inc. v. Rea*, 731 F. 3d 1248 (Fed. Cir. 2013), the Court found that the PTAB improperly corrected an acknowledged error in the Examiner's characterization of a reference, and supplied its own reasons to combine the references without giving Applicant an opportunity to respond.

In this case, the PTAB argued that exclusion of Suzuki was warranted because Suzuki was ambiguous as a consequence of a statement that the "apparent role of overexpression in HSP-27 has not been established, and remains controversial in oral SCC cells." (A19). Further, the Board argued that it was relevant that "Suzuki says absolutely nothing about radiotherapy." (A19) No comparable statements are found in the Examiner's arguments relating to obviousness in which the Examiner did not even mention Suzuki. A889-913.

The PTAB further stated "we conclude that Yonekura and Teimourian, which are supported by experimental data and teach a shared underlying mechanism by which inhibition of HSP 27 permits increased apoptosis of cancer cells provide a reasonable expectation of success when weighed against the ambivalent result of Suzuki." (A19-20.) This implies that the Suzuki contains no

experimental data, but this is not true. Furthermore, no prior statement criticizing Suzuki for lack of experimental results or ambivalent results, and no prior allegations concerning a “common underlying mechanism” were made in the record prior to the PTAB’s decision. Thus, the decision to exclude the Suzuki reference was made based on a new rationale for its exclusion, not found in the record before the Examiner and is thus a new ground of rejection.

Conclusion

For the foregoing reasons, Appellants submit that the rejection under 35 USC § 103(a) should be reversed as legally incorrect and as unsupported by substantial evidence. In the alternative, Appellants request remand so that the new grounds for rejection can be fully addressed.

Respectfully submitted,

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte CLAIRE RODRIGUEZ-LAFRASSE and ELIE HADCHITY

Appeal 2012-008236
Application 12/528,118
Technology Center 1600

Before DEMETRA J. MILLS, ERIC GRIMES, and JEFFREY N.
FREDMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal¹ under 35 U.S.C. § 134 involving claims to a method for treatment of squamous cell carcinoma characterized by elevated expression of hsp27 as compared to non-cancerous cells. The Examiner rejected the claims as failing to comply with the written description and enablement requirements and as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm-in-part.

¹ Appellants identify the Real Parties in Interest as The University of British Columbia and OncoGenex Technologies Inc. (*see* App. Br. 1).

Background

The Claims

1. A method for treatment of squamous cell carcinoma characterized by elevated expression of hsp27 as compared to non-cancerous cells of the same type in an individual suffering from the cancer, comprising treating a patient diagnosed with a squamous cell carcinoma with a combination of radio-therapy and a therapeutic agent that reduces the amount of hsp27 in the squamous cancer cells.

A. The Examiner rejected claims 1, 3, and 17 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement (Ans. 5-7).

B. The Examiner rejected claims 1-6 and 13-17 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement (Ans. 7-12).

Appeal 2012-008236
Application 12/528,118

C. The Examiner rejected claims 1, 2, 6, 13, and 15 under 35 U.S.C. § 103(a) as being obvious over Yonekura² and Teimourian³ (Ans. 12-14).

A. 35 U.S.C. § 112, first paragraph, written description

The Examiner finds that the “instant method embraces and contemplates the inhibition of hsp27 levels using a broad genus of inhibitors and the specification only describes the use of a single antisense oligonucleotide for use in the instantly claimed method” (Ans. 6). The Examiner finds that “it follows logically that a method of using any type of inhibitor cannot be adequately described without describing the inhibitor” (Ans. 6). The Examiner finds that “Applicants have not shown possession of the entire claimed genus of inhibitors that are capable of inhibiting the levels of hsp27 such that a treatment of squamous cell carcinoma” (Ans. 7).

Appellants contend that they “recognized the generic applicability of the invention regardless of the nature of the therapeutic agent and did not consider oligonucleotides to be the only way to accomplish the claimed method. In fact, a specific alternative to oligonucleotides, namely an antibody therapeutic, is disclosed” (App. Br. 3). Appellants contend that “at the time this application was filed, the art was aware of other methods and compositions for inhibiting hsp27. For example, Morino . . . shows

² Yonekura et al., *Interferon- γ downregulates Hsp27 expression and suppresses the negative regulation of cell death in oral squamous cell carcinoma lines*, 10 CELL DEATH DIFFERENTIATION 313-322 (2003).

³ Teimourian et al., *Down-regulation of Hsp27 radiosensitizes human prostate cancer cells*, 13 INT’L J. UROLOGY 1221-1225 (2006).

Appeal 2012-008236
Application 12/528,118

regulation of heat shock proteins, including hsp27, using flavonoid compounds” (App. Br. 3). Appellants contend that “Yonekura . . . shows the interferon- γ downregulates expression of Hsp27” (App. Br. 4). Appellants contend that “there were at the time of the invention a breadth of types of compounds known for accomplishing the stated function, and Applicants clearly had conceived of the invention” (App. Br. 4).

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s conclusion that the disclosure of the Specification does not demonstrate possession of the genus of “therapeutic agent[s] that reduce[] the amount of hsp27 in the squamous cancer cells” in the carcinoma treatment method of claim 1?

Findings of Fact

1. The Specification teaches that “the combination of hsp 27 antisense [oligonucleotide OGX-427] and radiation resulted in a dramatic change in the rate of tumor evolution” (i.e., the rate of tumor growth) (Spec. 6, 9-10). The Specification teaches that an OGX-427 oligonucleotide “was observed to reduce the amount of hsp27 protein in the cells after treatment with combined oligonucleotide and radiation therapy by over 68% as compared to treatment with radiation and a mismatch oligonucleotide control sequence” (Spec. 6).

2. The Specification teaches “[r]eduction in levels of active hsp27 can be achieved . . . by converting hsp27 to an inactive form, for example by sequestering hsp27 in an inactive complex such as with an anti-hsp27 antibody. Anti-hsp27 antibodies are known, for example from Tezel and Wax, J. Neuroscience 10:3553-3562 (2000)” (Spec. 3).

Appeal 2012-008236
Application 12/528,118

3. Yonekura⁴ teaches that the protein levels of Hsp27 in SCC [squamous cell carcinoma] cells are specifically reduced by IFN- γ treatment. However, expression of other molecular chaperones was not affected. IFN- γ -induced decrease in Hsp27 and cell death was not observed in any other cell lines tested, including HeLa. We therefore propose that Hsp27 plays a crucial role in the inhibition of apoptotic cell death in SCC cells.

(Yonekura 318, col. 2).

4. Morino⁵ teaches that “all the flavonoids used in this study (Figure 1) inhibited the expression of HSP27 . . . in human tumor cell lines” (Morino 266, col. 2).

5. Morino teaches that “Quercetin inhibited HSP27 expression in all the human tumor cell lines examined except H69 and PC-3 cells. Rutin inhibited HSP27 expression in three out of nine examined cell lines. (+)-Catechin, baicalein and wogonin inhibited HSP27 in two of nine, two of eight and four of eight cell lines, respectively” (Morino 266, col. 2 to 267, col. 1).

Principles of Law

“[T]he determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing

⁴ Yonekura et al., *Interferon- γ downregulates Hsp27 expression and suppresses the negative regulation of cell death in oral squamous cell carcinoma lines*, 10 CELL DEATH AND DIFFERENTIATION 313-322 (2003).

⁵ Morino et al., *Specific Regulation of HSPs in Human Tumor Cell Lines by Flavonoids*, 11 IN VIVO 265-70 (1997).

Appeal 2012-008236
Application 12/528,118

knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter.” *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005).

[W]e hold, in accordance with our prior case law, that (1) examples are not necessary to support the adequacy of a written description (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure.

Falko-Gunter Falkner v. Inglis, 448 F.3d 1357, 1366 (Fed. Cir. 2006). *See, e.g., LizardTech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005) (“it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention.”)

Analysis

We recognize the Examiner’s concern regarding the breadth of therapeutic agents encompassed by claim 1, since the claim is functionally drawn to the use of any therapeutic agent which reduces the amount of HSP27 in squamous cancer cells.

However, there is no requirement that the Specification describe every possible species encompassed by the claim. *See Utter v. Hiraga*, 845 F.2d 993, 998 (Fed. Cir. 1988) (“A specification may, within the meaning of 35 U.S.C. § 112, ¶ 1, contain a written description of a broadly claimed invention without describing all species that claim encompasses.”).

Appeal 2012-008236
Application 12/528,118

On the particularized facts in this situation, Appellants identify two structurally different species which are capable of inhibiting hsp27 in cells in the Specification, antisense oligonucleotides (FF 1) and anti-hsp27 antibodies (FF 2). The prior art of record teaches two additional, structurally unrelated species which also inhibit hsp27, interferon- γ in squamous cancer cells (FF 3) and flavonoids against several different cancer cell lines (FF 4-5). Thus, four entirely different classes of molecules were available, as of the filing date, which all function to inhibit hsp27 expression in cancer cells, and are therefore reasonably identified as a representative number of species to support the generic claim. *See Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.*, 598 F.3d 1336, 1350 (Fed. Cir. 2010) (“We held that a sufficient description of a genus . . . requires the disclosure of . . . a representative number of species falling within the scope of the genus”).

Conclusion of Law

The evidence of record does not support the Examiner’s conclusion that the disclosure of the Specification does not demonstrate possession of the genus of “therapeutic agent[s] that reduce[] the amount of hsp27 in the squamous cancer cells” in the carcinoma treatment method of claim 1.

B. 35 U.S.C. § 112, first paragraph, enablement

The Examiner finds that “there is no predictable correlation in the art for the role of overexpression or the lack of expression of hsp27 in squamous cell carcinomas” (Ans. 12). The Examiner finds that “[g]iven there is no guidance in the specification that would be considered enabling for the breadth of the claimed subject matter one of skill in the art would have to practice a substantial amount of trial and error experimentation, an

Appeal 2012-008236
Application 12/528,118

amount considered undue and not routine, to practice the instantly claimed invention” (Ans. 12).

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s conclusion that undue experimentation would have been required to practice the full scope of claim 1?

Findings of Fact

Breadth of the Claims

6. Claim 1 is drawn to a treatment method combining radiotherapy with any therapeutic agent which reduces the amount of hsp27 in squamous cancer cells.

Presence of Working Examples

7. The Specification teaches that “OGX-427 treatment dose-dependently inhibited Hsp27 expression [in SQ20B squamous cancer cells], up to 70% for 200 nM treatment and 90% for 2x200 nM at 24 hours post-transfection. MS control oligonucleotide did not modify Hsp27 expression” (Spec. 8).

8. The Specification teaches that “[c]ombining OGX-427 treatment with 30 Gy radiation significantly increased the inhibition of tumor growth. At the end of treatment, a respective 720 and 500% reduction of mean tumor volume was measured compared to the non-treated and only irradiated mice groups” (Spec. 12).

Amount of Direction or Guidance Presented

9. The Specification teaches that “[i]ncreasing dose of tumor radiation (30 Gy) in combination with OGX-427 treatment significantly

Appeal 2012-008236
Application 12/528,118

amplifies the inhibition of tumor growth, the increase of apoptosis and the decrease of tumor cell proliferation” (Spec. 13).

10. The Specification teaches that anti-hsp27 antibodies can be used to sequester hsp27 into an inactive complex (Spec. 3; FF 2).

11. The Specification teaches that “[s]pecific suitable antisense sequences are listed with DNA base[s] only in Seq. ID Nos. 1 - 90. Modifications to include RNA bases in place of the corresponding DNA base may be made” (Spec. 3).

State of the Prior Art and Unpredictability of the Art

12. The Examiner finds that “the state of the art linking a reduction in the overexpression of hsp27 and treatment for squamous cell carcinoma was unpredictable” (Ans. 9).

13. Suzuki⁶ teaches that “[o]ur results, however, showed that the effect of chemotherapy was good in patients whose cancers overexpressed HSP-27” (Suzuki 128, col. 2).

14. Suzuki teaches that “expression of HSP-27 seems to protect cells from apoptosis during inflammation, while down-regulation in dysplasia could impair the protective mechanism against mutagenesis induced by environmental factors, and so exaggerate the transformation of oral epithelial dysplasia into SCC” (Suzuki 128, col. 1).

15. Suzuki teaches that the “apparent role of overexpression of HSP-27 has not been established, and remains controversial in oral SCC

⁶ Suzuki et al., *Overexpression of heat shock protein 27 is associated with good prognosis in the patient with oral squamous cell carcinoma*, 45 BRITISH J. ORAL MAXILLOFACIAL SURGERY 123-129 (2007).

Appeal 2012-008236
Application 12/528,118

cells. The induction of expression of HSP-27 may prove useful in the treatment of carcinomas that do not express HSP-27” (Suzuki 129, col. 1).

16. Fortin⁷ teaches that in “our study, there was a significant relationship between neck relapse and absence of HSP-27 overexpression. These results corroborate the fact that HSP-27 overexpression has been associated with good prognosis. Moreover, HSP-27 overexpression is not associated with radioresistance” (Fortin 91, col. 2).

Quantity of Experimentation

17. The Examiner finds that “the instant invention invites further experimentation to find a correlation between inhibition of hsp-27 and a treatment effect in patients with squamous cell carcinoma” (Ans. 11).

Skill in the Art

18. The Examiner makes no finding regarding the skill in the art.

Principles of Law

Factors to be considered in determining whether a disclosure would require undue experimentation ... include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

⁷ Fortin et al., *Markers Of Neck Failure In Oral Cavity And Oropharyngeal Carcinomas Treated With Radiotherapy*, 23 HEAD & NECK 87-93 (2001).

Appeal 2012-008236
Application 12/528,118

Analysis

The analytical framework for determining whether claims fail to satisfy the enablement requirement balances the *Wands* factors to determine if undue experimentation would have been required to perform the reasonable scope of the claimed method at the time of filing of the Specification.

While claim 1 is broadly drawn to the use of any therapeutic agent which reduces the amount of hsp27 in squamous cancer cells (FF 6), the Specification teaches a large number of different oligonucleotide sequences for therapy as well as the use of antibodies (FF 9-11). There are working examples using both squamous cancer cell lines (FF 7) and a mouse squamous cell cancer xenograft model (FF 8).

While we agree with the Examiner that Suzuki suggests some level of unpredictability regarding the role of hsp27 (FF 15), Suzuki does not directly address the invention, which is drawn to the combination of an agent which reduces hsp27 levels along with radiotherapy. Instead, Suzuki simply teaches that high levels of hsp27 do not inhibit chemotherapy (FF 14). When Suzuki teaches that hsp27 protects cells from apoptosis (FF 13), this teaching supports the enablement of the invention, since presumably reduction of hsp27 levels in the SCC cells by the inventive method would enhance the desirable cell killing by the radiotherapy due to apoptosis, the goal desired by the invention.

The Examiner has not established that a large quantity of experimentation would have been required for the ordinary artisan to

Appeal 2012-008236
Application 12/528,118

perform this invention, in light of the teachings in the Specification (FF 17-18).

As we balance the factors relating to enablement, including the moderate scope of the claim, limited to a combination of radiotherapy and an hsp27 reducing therapeutic agent in squamous cancer cells, the presence of several working examples, the teachings in the Specification, relative to the prior art teaching of Suzuki that the role of hsp27 is controversial, we conclude that the balance of the *Wands* factors does not support the Examiner's finding that the claimed invention fails to comply with the enablement requirement.

Conclusion of Law

The evidence of record does not support the Examiner's conclusion that undue experimentation would have been required to practice the full scope of claim 1.

C. 35 U.S.C. § 103(a) over Yonekura and Teimourian

The Examiner finds that Yonekura teaches "methods of down regulating the expression of hsp-27 in oral squamous cell carcinoma lines using IFN-gamma treatments" (Ans. 12). The Examiner finds that Yonekura teaches that "overexpression of hsp-27 correlates with increased resistance to certain anti-cancer drugs and found that oral SCC cells that express lower levels of hsp-27 are more sensitive to the apoptotic stimuli" (Ans. 12). The Examiner finds that Yonekura teaches "that combining inhibitors of expression of hsp-27 such as IFN-gamma and other anticancer treatments would provide therapeutic benefits in methods of treatment of cancers" (Ans. 12-13).

Appeal 2012-008236
Application 12/528,118

The Examiner acknowledges that Yonekura does “not teach methods of treatment of patients diagnosed with squamous cell carcinoma and do[es] not teach a combination therapy using radiation” (Ans. 13). The Examiner finds that Teimourian teaches that “down-regulation of hsp-27 in combination with radiation may serve as a useful approach to induce apoptosis in tumor cells” (Ans. 13). The Examiner finds that Teimourian teaches “using an antisense compound to downregulate the expression of hsp-27 and found that a decrease in hsp-27 expression radiosensitizes said cells to become more radiation sensitive and emphasizes that inactivation of hsp-27 may be a promising approach to increased radiation sensitivity in cancer cells” (Ans. 13).

The Examiner finds it obvious “to use radiotherapy in combination with IFN-gamma as taught by Yonekura et al. because Teimourian et al. teach down-regulation of hsp27 in cancer cells radiosensitizes said cells to become more radiation sensitive therefore providing a promising approach to treatment of cancer cells that have become resistant to radiation therapy” (Ans. 13).

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s conclusion that the combination of Yonekura and Teimourian renders claim 1 obvious?

Findings of Fact

19. Yonekura teaches that “[i]nterferon- γ (IFN- γ) is considered a likely candidate for combination therapy in anticancer drug regimes” (Yonekura 313, col. 2).

Appeal 2012-008236
Application 12/528,118

20. Yonekura teaches that a “number of studies indicate that . . . Hsp27[] inhibits the apoptotic signaling pathway. . . . Here, we describe a novel downregulation of Hsp27 expression in response to IFN- γ treatment of oral SCC cells” (Yonekura 313, col. 2).

21. Yonekura teaches that “Hsp27-overexpressing clones displayed resistance to cisplatin-induced apoptosis (data not shown), consistent with earlier reports. Moreover, these recombinant constructs were significantly more resistant to IFN- γ -induced cell death than control cells” (Yonekura 316, col. 1).

22. Yonekura teaches that
Hsp27 in oral SCC cells plays a critical role in the negative regulation of apoptotic cell death. IFN- γ stimulates the cell death signal via its inhibitory effect of Hsp27, although not sufficiently to cause complete apoptotic cell death. In oral SCC cells, IFN- γ downregulates protein levels of Hsp27, and therefore possibly promotes the proapoptotic state by partially activating caspase-3
(Yonekura 317, col. 2).

23. Yonekura teaches that “IFN- γ -treatment augmented apoptotic cell death caused by certain inducers, including Verotoxin and cisplatin” (Yonekura 318, col. 1).

24. Yonekura teaches that “IFN- γ alone does not induce apoptosis, probably because it does not completely terminate Hsp27 expression and function. This study at the molecular level supports the potential therapeutic benefits of a treatment strategy combining IFN- γ with other anticancer drugs, such as cisplatin” (Yonekura 320, col. 1).

Appeal 2012-008236
Application 12/528,118

25. Teimourian teaches that “Hsp27 can also inhibit apoptosis through the direct inhibition of caspase activation” (Teimourian 1221, col. 2).

26. Teimourian teaches that “down-regulation of Hsp27 in combination with radiation may serve as a useful approach to induce apoptosis in tumor cells which develops new methods for treatment of cancers. We examined the possible role of Hsp27 in cellular resistance to radiation and investigated an Hsp27 antisense as a possible radiation sensitizer” (Teimourian 1222, col. 1).

27. Teimourian teaches that:

Although DNA-damaging therapies such as γ -radiation have been widely used for the treatment of numerous cancers, cells increasingly become resistant to consecutive administration of radiation; therefore, studies involving strategies to overcome this resistance by increasing cellular sensitivity to radiation therapy contribute[] a critical step for better cancer treatments. In this study, we demonstrated that the decreased expression of Hsp27 in radioresistant prostate cancer cells produced a decline in the survival curve; this suggests a possible use of Hsp27 antisense as a radiosensitizer.

(Teimourian 1224, col. 1).

28. Teimourian teaches that “[i]t should again be emphasized that, because overcoming radiation resistance is critical for better cancer treatment, inactivation of the stress-activated protein Hsp27 may be a promising approach to increased radiation sensitivity in cancer cells” (Teimourian 1224, col. 2).

Appeal 2012-008236
Application 12/528,118

Principles of Law

“The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). “If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability.” *Id.* at 417.

Analysis

Prima facie case

Yonekura teaches that hsp27 inhibits apoptosis (programmed cell death) in squamous cell carcinoma (SCC) cells (FF 20). Yonekura teaches that hsp27 plays a “critical role” in inhibiting apoptosis of oral SCC cells and that an agent (interferon- γ) which down-regulates hsp27 desirably activates apoptosis, helping the effectiveness of chemotherapeutic agents to kill the cancer cells (FF 22, 23). Yonekura directly suggests the combination of a compound which down-regulates hsp27 with other anticancer agents (FF 24).

Teimourian also uses an agent, here an oligonucleotide, which down-regulates hsp27 and specifically teaches that this agent may be useful in combination with radiation treatment of cancer cells (FF 26, 28). Teimourian teaches that radiation combined with decreased expression of hsp27 resulted in reduced survival of cancer cells; that is, better success in treatment of cancer (FF 27).

Applying the *KSR* standard of obviousness to the findings of fact, we conclude that the person of ordinary creativity would have predictably combined radiation and hsp27 down-regulation compounds for the treatment

Appeal 2012-008236
Application 12/528,118

of squamous cell carcinomas since Yonekura teaches that such compounds sensitize squamous cell carcinoma cells for apoptosis induced by other treatments (FF 20-24) and Teimourian teaches that “inactivation of the stress-activated protein Hsp27 may be a promising approach to increased radiation sensitivity in cancer cells” (Teimourian 1224, col. 2; FF 28). Such a combination is merely a “predictable use of prior art elements according to their established functions.” *KSR*, 550 U.S. at 417.

Appellants contend that “Fortin 2001 teaches that Hsp27 overexpression has not been associated with radioresistance. Thus a person skilled in the art, taking this statement at face value, would have no reason to imagine that the combination said to be obvious would offer any benefit, and in fact could consider it an express teaching away” (App. Br. 8).

We are not persuaded. In *Gurley*, the court found that the “degree of teaching away will of course depend on the particular facts” *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994). Appellants solely rely upon Fortin’s citation of a 1985 paper regarding the sensitivity of cell lines to radiation (*see* Fortin 93, footnote 29) which never specifically teaches or demonstrates that squamous cell carcinoma cells are resistant to radiation, or even that the cells tested in the cited paper overexpressed hsp27. Appellants, in fact, candidly acknowledge that “the statement in the Fortin 2001 reference is wholly unsupported by the document cited therein. This reference is completely silent about Hsp27” (App. Br. 8, note 3).

By contrast, Appellants’ own Specification recognizes that the ordinary artisan was aware that “[t]reatment for squamous cell cancer may involve treatment with radiation with or without surgical removal of the

Appeal 2012-008236
Application 12/528,118

tumor mass” (Spec. 1). In addition, the Teimourian reference expressly suggests the combination of hsp27 down-regulating agents with radiation therapy to increase radiation sensitivity of cancer cells (FF 26, 28) while Yonekura also expressly suggests combination therapy with hsp27 down-regulating agents and other cancer treatments (FF 24).

Therefore, the balance of the facts does not support Appellants’ position that the prior teaches away from the use of an hsp27 down-regulation compound and radiation therapy in view of the express suggestion of such therapy by Teimourian (FF 28).

Appellants contend that “the state of the art at the time would not have viewed this combination to offer any benefit, and thus one skilled in the art would not have made the combination” (Reply Br. 5).

We are not persuaded. This argument is flatly contradicted by the Examiner’s cited art, where Yonekura teaches “the potential therapeutic benefits of a treatment strategy combining IFN- γ with other anticancer drugs, such as cisplatin” for squamous cell carcinoma cells (Yonekura 320, col. 1; FF 24) while Teimourian teaches that “[i]t should again be emphasized that, because overcoming radiation resistance is critical for better cancer treatment, inactivation of the stress-activated protein Hsp27 may be a promising approach to increased radiation sensitivity in cancer cells” (Teimourian 1224, col. 2; FF 28). Both Yonekura and Teimourian share an underlying mechanism of improving apoptosis by reducing HSP 27 levels, thereby suggesting the application of each therapeutic modality with agents which reduce HSP 27 levels (FF 19-28).

Appeal 2012-008236
Application 12/528,118

Applying Teimourian's approach to prostate cancer cells, in light of Yonekura's teaching that inactivation of hsp27 as part of a viable combination therapy for cancer cells, would have certainly motivated the ordinary artisan to perform the combined radiation and hsp27 down-regulation treatment, performed by Teimourian on prostate cancer cells, on squamous cell carcinoma cells (FF 19-28).

We appreciate that Suzuki teaches that "the effect of chemotherapy was good in patients whose cancers overexpressed HSP-27" (Suzuki 128, col. 2; FF 14), but Suzuki is ambiguous, also teaching that the "apparent role of overexpression of HSP-27 has not been established, and remains controversial in oral SCC cells. The induction of expression of HSP-27 may prove useful in the treatment of carcinomas that do not express HSP-27" (Suzuki 129, col. 1; FF 15). Further, as Appellants note, Suzuki says "absolutely nothing about radiotherapy" (Reply Br. 4).

By contrast, Yonekura teaches that "Hsp27 in oral SCC cells plays a critical role in the negative regulation of apoptotic cell death. IFN- γ stimulates the cell death signal via its inhibitory effect of Hsp27" (Yonekura 317, col. 2; FF 22). Teimourian teaches that "down-regulation of Hsp27 in combination with radiation may serve as a useful approach to induce apoptosis in tumor cells which develops new methods for treatment of cancers" (Teimourian 1222, col. 1; FF 26).

As we balance these prior art teachings, we conclude that Yonekura and Teimourian, which are supported by experimental data and teach a shared underlying mechanism by which inhibition of HSP 27 permits increased apoptosis of cancer cells, provide a reasonable expectation of

Appeal 2012-008236
Application 12/528,118

success when weighed against the ambivalent results of Suzuki. In *Kubin* the court found that “this court [in *O’Farrell*] stated: ‘[o]bviousness does not require absolute predictability of success ... all that is required is a reasonable expectation of success.’” *In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009).

Conclusion of Law

The evidence of record supports the Examiner’s conclusion that the combination of Yonekura and Teimourian renders claim 1 obvious.

SUMMARY

In summary, we reverse the rejection of claims 1, 3, and 17 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

We reverse the rejection of claims 1-6 and 13-17 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement (Ans. 7-12).

We affirm the rejection of claim 1 under 35 U.S.C. § 103(a) as being obvious over Yonekura and Teimourian. Pursuant to 37 C.F.R. § 41.37(c)(1), we also affirm the rejection of claims 2, 6, 13, and 15, as these claims were not argued separately.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED-IN-PART

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte CLAIRE RODRIGUEZ-LAFRASSE and ELIE HADCHITY

Appeal 2012-008236
Application 12/528,118
Technology Center 1600

Before DEMETRA J. MILLS, ERIC GRIMES, and JEFFREY N.
FREDMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON REQUEST FOR REHEARING

Appellants have requested rehearing of the decision entered December 20, 2012. That decision affirmed the Examiner's rejection of claims 1, 2, 6, 13, and 15 under 35 U.S.C. § 103(a).

Appellants' request has been granted to the extent that the decision has been reconsidered, but such request is denied with respect to making any modifications to the decision affirming the Examiner's rejection under 35 U.S.C. § 103(a).

Appeal 2012-008236
Application 12/528,118

DISCUSSION

Argument 1

Appellants contend that to “the extent that the Board has supplied a partial rationale for considering less than all of the art of record, this must be viewed as a new ground for rejection, and does not permit a simple affirmance of the rejection” (Req. Rehearing 2).

We have reviewed our Decision in light of these arguments. However, we are not persuaded that our Decision was in error or constitutes a “New Ground of Rejection.” We considered the evidence presented by the Examiner, represented by the Teimourian and Yonekura references (*see, e.g.,* Final Rej. 21-22; Dec. 16-17), balanced against the rebuttal evidence consisting of Fortin and Suzuki presented by Appellants (*see* Dec. 17, 19; App. Br. 8; Reply Br. 5). We solely relied upon evidence presented by either the Examiner in the Final Rejection or submitted by Appellants. Appellants “neither point[] to specific facts found by the Board but not by the examiner, nor illustrate[] how any such facts formed the basis of the Board’s rejection.” *In re Adler*, 733 F.3d 1322, 1327 (Fed. Cir. 2013). “While the Board’s explanation may go into more detail than the examiner’s, that does not amount to a new ground of rejection.” *Id.* at 1328. “The Board cannot be said to have presented a new ground of rejection simply by elaborating on the examiner’s rejection or by using different words. *See In re Oetiker*, 977 F.2d 1443, 1445-46 (Fed.Cir.1992).” *Hyatt v. Doll*, No. 2007-1066, slip op. at 27 (Fed. Cir. Aug. 11, 2009).

Appeal 2012-008236
Application 12/528,118

Argument 2

Appellants contend that the “Board has offered no explanation of why the facts found with respect to the Fortin reference were not considered in reaching the conclusion of obviousness” (Req. Rehearing 5). Appellants further contend that “the justification for omitting Suzuki from the analysis is in error” (Req. Rehearing 5).

We find these arguments unpersuasive. We specifically explained, in our Decision, why we gave little weight to the Suzuki and Fortin references (Dec. 17, 19-20). In particular, we explained that:

Appellants solely rely upon Fortin’s citation of a 1985 paper regarding the sensitivity of cell lines to radiation (*see* Fortin 93, footnote 29) which never specifically teaches or demonstrates that squamous cell carcinoma cells are resistant to radiation, or even that the cells tested in the cited paper overexpressed hsp27. Appellants, in fact, candidly acknowledge that “the statement in the Fortin 2001 reference is wholly unsupported by the document cited therein. This reference is completely silent about Hsp27” (App. Br. 8, note 3).

(Dec. 17). Further, our Decision clearly considered the Suzuki reference (*see* Dec. 9, 10, 19), specifically applying our scientific and legal expertise in balancing the teachings of Yonekura, Teimourian, and Suzuki in the obviousness rejection (*see* Dec. 19-20). That Appellants disagree with our conclusion does not demonstrate any point of fact or law which we overlooked.

SUMMARY

We have carefully reviewed the original opinion in light of Appellants' request, but we find no other point of law or fact which we overlooked or misapprehended in arriving at our decision. Therefore, Appellants' request has been granted to the extent that the decision has been reconsidered, but such request is denied with respect to making any modifications to the decision affirming the Examiner's rejection under 35 U.S.C. § 103(a).

DENIED

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Certificate of Service

I certify that on August 15, 2014, I electronically filed the foregoing BRIEF FOR APPELLANT with the Court's CM/ECF filing system, which constitutes service, pursuant to Fed. R. App. P. 25(c)(2), Fed. Cir. R. 25(a) and the Court's Administrative Order Regarding Electronic Case Filing 6(A) (May 17, 2012) to all registered CM/ECF users.

/s/ Marina T. Larson

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